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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/464,795	12/16/1999	NING ZHANG	PXE-007.US	8087

7590 10/05/2004

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EXAMINER	
SHUKLA, RAM R	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 10/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/464,795	ZHANG ET AL.	
	Examiner	Art Unit	
	Ram R. Shukla	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38,40,41,43,45,46,49 and 65-68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38,40,41,43,45,46,49 and 65-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 December 1999* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/12/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of the species- first control element derived from heme oxygenase, a second control element derived from cytochrome p450 1A1 and a third control element derived from PPRE in the reply filed on 7/9/04 is acknowledged. The traversal is on the ground(s) that it is improper for the office to refuse to examine that which applicants regard as their invention. This is not found persuasive because, first, applicants have not been refused examination, therefore the arguments are irrelevant. Second, all the genes listed are not true species, the genes have very different promoter structure and searching for one gene would not yield art relevant to another. Therefore, there will be undue search and examination burden for considering all the genes listed. Applicants are reminded that the search would not only require the search for an animal but also for different genes listed and such will be an undue burden. The requirement is still deemed proper and is therefore made FINAL.

2. Claims 38, 40, 41, 43, 45, 46, 49, and 65-68 are pending and under consideration.

Claim Rejections - 35 USC § 101

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 38, 40, 41, 43, 45, 46, 49, and 65-68 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

When determining whether an applicant has described the utility of invention, one has to determine whether the applicant has described a well-established utility. If not, has the application made any assertion of specific, substantial and credible utility. A credible utility is assessed from the standpoint of whether a person of ordinary skill in the art would accept that the recited or disclosed invention is

currently available for use. In contrast to general utility, a specific utility will be specific to the claimed subject matter. A substantial utility defines a real world utility of the invention and utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context use are not substantial utility (see utility guidelines, in Federal Register January 5, 2001, Volume 66, Number 5, Pages 1092-1099).

In the instant case of a transgenic mouse comprising two or three constructs that comprise a control element of heme oxygenase driving the expression of a light emitting polypeptide, a second construct comprising a control element of cytochrome p450 1A1 driving the expression of a light emitting polypeptide and a third construct comprising peroxisome proliferation response element driving the expression of a light emitting polypeptide, the utility is to determine the effect of an analyze on gene expression. However, the specification does not teach what would be utility of a mouse that has three different constructs each comprising a different promoter and what would be the utility of a compound or analyte which affects these promoters. The specification does not describe any specific and or substantial utility for such a transgenic mouse or for a compound that affects the expression from three different control elements. While an artisan could understand that a compound could be identified that affected the expression of one control element in a mouse that comprised one control element, however, an artisan would not know what was the specific use of a mouse that comprised two or three control elements that were not related in structure or function. It's noted that heme oxygenase is an enzyme in heme catabolic pathway whereas cytochrome p450 is a drug-metabolizing enzyme and peroxisome proliferation responsive element is associated with free radical metabolism.

It is emphasized that the specification as filed does not describe a specific utility for the claimed transgenic mouse (comprising two or three constructs as recited).

Therefore, the claimed transgenic mouse is not supported by either a specific and/or substantial utility, since no function can be ascribed to the gene.

It is noted that patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. See Brenner v. Manson , 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.") Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 38, 40, 41, 43, 45, 46, 49, and 65-68 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for reasons of record set forth in the previous office action of 2-1-01, 9-13-01, 8/27/02 and 5/21/03 and as discussed below.

The amendment to claim 38 lists several genes, of which applicants elected heme oxygenase whose control element is comprised in the first expression cassette, while a second control element derived from cytochrome p450 1A1 is comprised in the second cassette. For claim 65, applicants elected PPRE control element.

It is noted that recitation of specific genes does not reduce or address the description issues, rather raise additional issues. For example, regarding a control element of heme oxygenase, the genus will be very broad because the heme oxygenase gene has multiple isozymes which have different structures, comprises multiple response elements and the function of heme oxygenase promoter varies in

various animals. For example, a rat heme oxygenase promoter is responsive to heat shock in vitro whereas a human promoter is not (see the abstract in Shibahara et al. Eur J Bichem 179 :557-563, 1989). The claimed transgenic mouse would not just have first construct, it would have second construct which comprises a cyt p450 1A1. There is no description in the specification what would be the characteristics of a transgenic mouse in whose genome two constructs have been integrated which could have integrated in or near the endogenous genes of the mouse and could have disrupted the function of the endogenous control element and one could not predict whether a viable transgenic mouse as claimed could even be produced. In other words, the claimed transgenic mouse which represents a genus itself could not be predictably described in view of the unpredictability of the art of transgenesis.

As discussed in the previous office actions, it is reiterated that applicants have described in the specification a method of producing transgenic mouse, not the transgenic mouse, the claimed invention. Disclosure of method of making a product is not the disclosure of a product. Additionally, a transgenic mouse is not a mixture of DNA constructs and cells in a test tube, rather it is an entity and since presence of the DNA construct, interaction between the DNA construct and the cells of the mouse and the interaction of the expression product of the DNA construct with the cell, all play a role in the characteristics of the transgenic mouse produced and in view of the unpredictability of the production of a transgenic mouse, just disclosing a transgenic mouse comprising a certain DNA construct is not a sufficient description of a mouse. It is reiterated that considering the fact the art of making transgenic animals is highly unpredictable, the phenotype(s) of the claimed animals cannot be predicted because. As discussed in the previous office actions, the art teaches that phenotype of a transgenic mouse cannot be predicted(see Wood (Comparative Medicine 50 (1): 12-15, 2000).

In conclusion, as discussed in the previous office actions, the limited disclosure in the specification is not deemed sufficient to reasonably convey to one skilled in the art that Applicants were in possession of the huge genera recited in the claims at the time the application was filed. Thus it is concluded that the

written description requirement is not satisfied for the claimed genera of the invention.

7. Claims 38, 40, 41, 43, 45, 46, 49, and 65-68 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record set forth in the previous office action of 2-1-01, 9-13-01, 8/27/02 and 5/21/03 and as discussed below.

As discussed in the written description requirement, claims have been amended by reciting specific genes whose control elements are comprised in the constructs, however recitation of specific genes does not reduce or address the enablement issues, rather raise additional issues. For example, heme oxygenase gene has multiple isozymes which have different structures, comprises multiple response elements and the function of heme oxygenase promoter varies in various animals. For example, a rat heme oxygenase promoter is responsive to heat shock in vitro whereas a human promoter is not (see the abstract in Shibahara et al. Eur J Biochem 179 :557-563, 1989). While the art of record teaches transgenic mouse that expresses heme oxygenase I promoter regulated expression of luciferase (Contag et al. Journal of Perinatology 21:S119-S124, 2001; Zhang et al. Oxygen transport to tissue, XXI 1999), there is no guidance whether the expression of a second promoter driving the expression of the same light generating polypeptide could be achieved in the same mouse. Additionally, there is no evidence that an artisan could produce a transgenic mouse with fragments of the promoters and the specification does not provide any guidance what fragments would be active in vivo, particularly when more than one constructs are being expressed. Additionally, in view of the unpredictability of transgenesis, an artisan could not predict whether a transgenic mouse comprising three different construct with three different promoters driving the expression of a light generating polypeptide could be produced, what would be its characteristics and how would an artisan use the mouse for determining the effect of a compound that altered the expression by the

promoters or control elements. For example, if one compound affected all the three control or two control elements, how would an artisan determine which control element was affected and to what extent. Further, in addition to the unpredictability of producing a transgenic mouse as claimed, it would be unpredictable as to what would be the effect of an exogenous control element being present in the mouse while the endogenous control element was active. Furthermore, the effect of control elements from different species could not be predicted. It is noted that applicants have just provide an ideas and have not provide specific details how would the transgenic mouse be used and for what?

It is noted that patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. See Brenner v. Manson , 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.") Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.

In summary, since the of the art of making of transgenic mice is highly unpredictable and unless a transgenic mouse has been produced, one can not predict what will the characteristics of the transgenic mouse comprising a given panel of expression constructs and therefore, an artisan would not know how to use the claimed transgenic mouse in claimed methods.

8. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (571) 272-0735 . The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (571) 272-

0804. The fax phone number for TC 1600 is (703) 872-9306. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the Dianiece Jacobs whose telephone number is (571) 272-0532.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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